CDK4 IS A TARGET OF c-MYC

ABSTRACT

The prototypic oncogene *c-MYC* encodes a transcription factor, which can drive proliferation by promoting cell cycle re-entry. However, the mechanisms through which c-MYC achieves these effects have been unclear. Using serial analysis of gene expression (SAGE), we have identified the cyclin dependent kinase 4 (*CDK4*) gene as a transcriptional target of c-MYC. c-MYC induced a rapid increase in *CDK4* mRNA levels through four highly conserved c-Myc binding sites (MBS) within the *CDK4* promoter. Cell cycle progression is delayed in *c-MYC*-deficient RAT1 cells, and this delay was associated with a defect in CDK4 induction. Ectopic expression of *CDK4* in these cells partially alleviated the growth defect. Thus, *CDK4* provides a direct link between the oncogenic effects of c-*MYC* and cell cycle regulation.